Yellow Fever

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify cases of yellow fever associated with travel and prevent further spread of the disease within the United States.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction.**
2. Hospitals: **immediately notifiable to local health jurisdiction.**
3. Laboratories: isolation of yellow fever virus, or detection of viral antigen, antibody or nucleic acid notifiable to local health jurisdiction of the patient's residence within 2 work days.
4. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. Alert CDES about possible cases.
2. Facilitate transport of specimens (e.g., serum) to the Washington State Department of Health Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDES prior to submitting specimens (206-418-5500).
3. Report all *confirmed* and *probable* cases to CDES (see definitions below). Complete the Yellow Fever case report form (http://www.doh.wa.gov/notify/forms/yellow.pdf) and enter the data into the Public Health Issues Management System (PHIMS) as "Yellow Fever."

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

Yellow fever is a very rare cause of illness in travelers. The disease is known to occur only in certain regions of Africa and South America.

A. Etiological agent

The etiologic agent of yellow fever is a RNA virus of the genus *Flavivirus* and family Flaviviridae.

B. Description of Illness

The disease typically begins with fever, headache, muscle aches, nausea and vomiting. The pulse may be slow and weak out of proportion to the elevated temperature (the Faget sign). Jaundice is moderate early in the disease and is intensified later. Albuminuria, sometimes pronounced, helps to distinguish yellow fever from other causes of viral hepatitis. Leukopenia appears early and is most pronounced about the fifth day. Most

infections resolve at this stage. After a brief remission of hours to a day, some cases progress into the ominous stage of intoxication manifested by hemorrhagic symptoms including epistaxis, gingival bleeding, hematemesis (coffee-ground or black), melena, and liver and renal failure. Twenty to 50% of jaundiced cases are fatal.

C. Yellow fever in Washington State

No cases of yellow fever have been reported in Washington in over 50 years.

D. Vectors and Reservoirs

Yellow fever exists in nature in two transmission cycles, a sylvatic or jungle cycle that involves mosquitoes and non-human primates, and an urban cycle involving *Aedes aegypti* mosquitoes and humans. Sylvatic transmission is restricted to tropical regions of Africa and South America, where a few hundred cases occur annually, most frequently among young adult males who are occupationally exposed in forested areas. Urban yellow fever has not occurred in the western hemisphere since the 1950s. However, reinfestation in many areas (including the southern United States) with *Ae. aegypti* raises the possibility of renewed urban yellow fever transmission should an infected person return to those areas. Humans have no essential role in transmission of jungle yellow fever or in maintaining the virus, but are the primary amplifying host in the urban cycle.

E. Modes of Transmission

Yellow fever is acquired through the bite of an infected mosquito.

F. Incubation Period

Three to six days.

G. Period of Communicability

Yellow fever is not directly transmitted from person to person, but can be indirectly transmitted from person to person via a mosquito vector as described above in the urban transmission cycle. Blood of patients is infective for mosquitoes shortly before onset of fever and for the first 3 to 5 days of illness. The disease is readily transmitted where many susceptible people and abundant vector mosquitoes coexist. Once infected, mosquitoes remain so for life.

H. Treatment

Treatment is supportive, often involving hospitalization with intensive care therapy.

3. CASE DEFINITION

A. Clinical Description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and in some instances, renal failure, shock, and generalized hemorrhages.

B. Laboratory Criteria for Diagnosis

1. Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded, or

2. Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

C. Case Definition (1997)

1. Probable: a clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., ≥ 32 by complement fixation, ≥ 256 by immunofluorescence assay, ≥ 320 by hemagglutination inhibition, ≥ 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)
2. Confirmed: a clinically compatible case that is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Laboratory diagnosis is often made by demonstrating specific immunoglobulin M (IgM) in early sera or a rise in titer of specific antibodies in paired acute and convalescent sera. Serologic cross-reactions occur with other flaviviruses. Recent infections can often be distinguished from vaccine immunity by complement fixation testing.

Laboratory diagnosis is also made by demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

B. Tests Available at the Washington State Department of Health Public Health Laboratories (PHL)

PHL does not perform testing for yellow fever but will forward specimens to the CDC for testing. Please contact CDES for approval prior to submitting specimens.

C. Specimen Collection

Serum should be refrigerated and transported cold. Specimens should be submitted with a completed DOH PHL Virus Examinations form available at: http://www.doh.wa.gov/EHSPHL/PHL/Forms/VirusExams.pdf.

Please call PHL for instructions for shipping specimens other than serum.

5. ROUTINE CASE INVESTIGATIONS

Since yellow fever is an extremely rare disease, call CDES to discuss the case investigation. Interview the case and others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

If the case tests positive for yellow fever at a laboratory other than Public Health Laboratories or CDC, facilitate transport of the specimen to PHL for further testing.

B. Identify Potential Sources of Infection

Obtain a travel history and ask about mosquito exposures during the likely exposure period.

C. Identify Potentially Exposed Persons

Identify other persons who traveled with the case. Determine if the patient donated blood during the communicable period. If the patient donated blood, inform the blood bank of the potential exposure.

6. CONTROLLING FURTHER SPREAD

A. Infection Control / Case Management

1. Hospitalized patients should be cared for using standard precautions.
2. Patients being treated for yellow fever in the United States should be sequestered from mosquitoes while viremic to avoid urban transmission. Given that *Ae. aegypti,* the principle mosquito vector, is not endemic to Washington State, the risk of the case infecting mosquitoes which could subsequently infect other humans is very low.

B. Contact Management:

None, since yellow fever is not directly transmitted from person to person.

C. Management of Other Exposed Persons:

If other persons who traveled with the case have symptoms consistent with yellow fever, refer them to a health care provider and arrange for laboratory testing.

7. MANAGING SPECIAL SITUATIONS

Not applicable

8. ROUTINE PREVENTION

See http://www.cdc.gov/ncidod/dvbid/yellowfever/YF_Prevention.html.

A. Immunization Recommendations

For information about yellow fever vaccine recommendations, please view the 2002 Yellow Fever Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2002 at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5117a1.htm.

B. Prevention Recommendations

When traveling in areas where yellow fever occurs (i.e., areas of Africa and South America), persons should avoid mosquito bites by:

- **Using mosquito repellant.** The most effective mosquito repellents contain the EPA approved active ingredients DEET (N, N-diethyl-m-toluamide), picaridin, oil of lemon eucalyptus, or IR3535. These products come in lotions, creams, gels, sprays, and towelettes. Read and follow instructions on the label. Do not over use repellents. Take special care when using repellent on children.
    - Additional information regarding the use of mosquito repellents can be found on the CDC website at: http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm and http://www.cdc.gov/ncidod/dvbid/westnile/RepellentUpdates.htm
- **Wearing Proper Clothing to Reduce Mosquito Bites.** When weather permits, wear long-sleeves, long pants and socks when outdoors. Mosquitoes may bite through thin

clothing, so spraying clothes with repellent containing permethrin or another EPA-registered repellent will give extra protection. Don't apply repellents containing permethrin directly to skin.

- **Be Aware of Peak Mosquito Hours.** The peak biting times for many mosquito species is dusk to dawn, however *Aedes aegypti*, the main vector of yellow fever virus, feeds during the daytime. Take extra care to use repellent and protective clothing during daytime as well as evening and early morning or consider avoiding outdoor activities during these times when in areas where yellow fever is a risk.

ACKNOWLEDGEMENTS

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UPDATES

March 2008: In Section 1C, the guideline for timeliness of initiating an investigation was removed.

July 2008: In Section 8B, IR3535 was added as a safe and effective mosquito repellent.